REMARKS

Upon entry of the present amendment, claims 1-3, 5-8, 39, 40, 43, 45, 46, 51, 52, and 55-57 are pending. Claim 9 has been canceled.

No new matter has been added.

I. Rejections under 35 U.S.C. § 103

Claims 1-3, 5-7, 40, 43, 46, 51, 52, and 57-59 were rejected for obviousness over de la Monte et al. and Lavaissiere et al. in view of Wer-Remers et al. On page 4, lines 7-14, of the Office Action, the Examiner states:

> Teachings of Lavaissiere et al. and De la Monte et al. suggest that the HAAH expression is not limited to a specific tumor or tumor with specific tissue origin but could be applied to many diverse tumors such as CNS and HCC. As for detecting a tumor marker over-expressed in tissue, Wer-Remers et al. teach one skilled in the art tests whether a tumor over-expressed could be detected in bodily fluid, thus providing motivation to one in ordinary skill to look for bodily fluid overexpression of a cancer marker because detecting a cancer biomarker in bodily fluid such as serum would be much less invasive than biopsy of brain, for example.

Claims 1-3, 5-7, 40, 43, 46, 51, 52, 58, and 59 are directed to diagnosing a malignant neoplasm by testing a bodily fluid from a mammal. Neither Lavaissiere et al. nor de la Monte et al. describe or suggest testing a bodily fluid. The Examiner relies on Wer-Remers et al. for a motivation to look to bodily fluids rather than tissue.

First, there is no reason or suggestion to combine Lavaissiere et al. and de la Monte et al. with Wer-Remers et al., because the type of proteins described and disease indications described by Wer-Remers et al. are significantly different from those described by Lavaissiere et al. or de la Monte et al. None of the references contain any explicit or implicit reasons to combine them. Not all tumor markers are equal or even equivalent in their structure, function, or distribution.

The protein described by Lavaissiere et al. and de la Monte et al. is an enzyme, whereas Wer-Remers et al describes a transmembrane cell-adhesion glycoprotein. One of skill in the art would have no reason to believe that an aspartyl (asparaginyl) beta-hydroxylase enzyme would behave like CD44 in its expression or distribution within the body.

Second, the Examiner is reminded that prior art references must be read as a whole and considered in their entirety. Consideration must be given to where the reference diverges and teaches away from the prior art. W.L. Gore & Assocs. V. Garlock, 721 F.2d 1540, 1550. In this case, Wer-Remers et al. taken in its entirety teaches away from the claimed invention. Wer-Remers et al. undertook to evaluate whether tissue expression of CD44 variants and serum levels correlate with one another and whether serum levels of soluble variants have clinical value to evaluate disease. These researchers concluded that serum levels of soluble CD44 or variants thereof did not have diagnostic value: "sCD44v6 serum concentration is independent of CD44v6 expression in the primary tumor " (page 793, col. 2, paragraph 1); "neither sCD44 nor sCD44v6 has clinical value as a tumor marker" (page 793, col. 2, paragraph 3, of Wer-Remers et al.); and "sCD44 and sCD44v6 concentrations showed no correlation to tumor burden or CD44v6 tissue expression" (abstract of Wer-Remers et al.). In contrast, Applicants have shown that an increase in HAAH level in bodily fluids is a valuable and reliable diagnostic tool.

Moreover, the prior art must suggest not only that a certain approach may be tried, but also that there would be a reasonable expectation of success: "Both the suggestion and the expectation of success must be found in the prior art, not in the applicant's disclosure." (emphasis added) In re Dow Chemical Co. 837 F.2d 469, 473. " Thus, although the Wers-Remers reference may suggest testing a bodily fluid, it in no way suggests an expectation of success in diagnosing malignancies. In fact, it suggests just the opposite – that serum levels are of little or no clinical value. Applicants therefore request withdrawal of this rejection.

Claim 57 is drawn to a method of diagnosing pancreatic cancer. The Examiner's rationale for rejecting this claim appears to be that given the description of elevated HAAH in hepatocellular carcinoma (HCC) and CNS tumors, it would be obvious to diagnose any tumor by measuring HAAH level. Many tumor markers are tissue specific or tumor specific. Although some markers are useful to diagnose many different tumor types, exactly which different types cancers are diagnosed with a given marker are not predictable and must be established by empirical data.

Most markers are not useful for detection of a broad range of tumor types, and there is no indication in the cited art that HAAH is useful to generally diagnose any type of malignancy. One of skill in the art would therefore not predict that a tumor marker for HCC and CNS cancer would also be of diagnostic value for pancreatic cancer. Neither Lavaissiere et al. nor de la Monte et al. suggest that HAAH is overexpressed in any other tissue except HCC or CNS cancers, respectively. In view of the absence of any suggestion of specifically diagnosing pancreatic cancer by measuring HAAH, this rejection must be withdrawn.

Claim 39 was rejected for obviousness over de la Monte et al., Lavaissiere et al., in view of Wers-Remers, in further view of Huse et al. This claim depends on claim 1 (detecting HAAH in bodily fluids to diagnose malignancy) and further requires that the antibody be a single chain antibody. As is discussed above, claim 1 is nonobvious over the cited art. Neither de la Monte et al. nor Lavaissiere et al. describe or suggest testing bodily fluid, and the Huse et al. reference also fails to do so. If anything, Wer-Remers et al. indicate that testing the serum for soluble proteins related to a tumor marker that is overexpressed in tissue would be of little or no clinical value. Withdrawal of this rejection is therefore requested.

I. Rejections under 35 U.S.C. § 112

Claim 9 was rejected for lack of enablement. Claim 9 has been canceled; therefore this rejection can now with withdrawn.

Claims 7, 8, 40, 45, 55, 56, and 59 were rejected for failing to comply with the enablement requirement. On page 3, lines 1-7, the Examiner states:

> This rejection is maintained because the deposit appears to be made **after the effective filing date of the application** for patent in the United States. A verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed. (emphasis in the original)

Applicants hereby submit a Statement of Jack R. Wands Regarding Biological Culture Deposit indicating that the antibody-producing hybridoma cell lines described in the specification as filed are the same as those deposited with the ATCC and that the cell lines were in Applicants' possession at the time the patent application from which this divisional case claims priority was filed. Applicants believe that they are in full compliance with the requirements for biological material deposit practice in conjunction with a patent application. Withdrawal of this rejection is therefore respectfully requested.

CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested.

A petition for one-month extension of time and a check in the amount of $110.00 is enclosed to cover the petition fee pursuant to 37 C.F.R. § 1.17(a)(3). The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21486-032DIV1.

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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